REMARKS

Upon entry of this amendment, claims 1, 2, 5-8, 11, 12, 16-19, 22, 25, 26, and 33-38 will be pending. Applicants thank the Examiner for establishing an RCE, and for withdrawing certain objections and rejections set forth in the previous office action. The support for the amendment and the new claims can be found throughout the specification and in the previously examined claims, and therefore no new matter has been introduced by this amendment. More specifically, claims 1 and 2 were amended to incorporate canceled claims 9, 10, and 24, which were original claims to this application. Support for new claim 33 can be found in the original claim 19. Support for new claims 34 to 37 can be found in the specification at, among other places, page 34, line 10 to page 38, line 8, Example 3. Support for new claim 38 can be found in the specification at page 33, line 16 to page 34, line 9. Applicants note that the specification and claims included typographical errors, using "neuropoetic" rather than the correct spelling "neuropoietic" to describe certain cytokines. The claims were amended to correct this typographical error, which correction introduces no new matter.

I. Specification

The specification was objected to because of the reference to patent applications. Applicants have amended the specification to update the status of the referenced applications. The Examiner points to page 1, lines 14-15, which has been amended to reflect the current status of the applications. The Examiner also points to page 21, lines 8-9. The status of these applications was updated by Applicants' amendment dated March 11, 2003. The Examiner also points to page 25, line 25. The application cited therein is still pending. Applicants will make the necessary amendments before the issuance of this application as a patent. Lastly, the Examiner points to page 35, line 11, which has been amended to reflect the current status of the applications.

II. Claim objections

The Examiner objects to claims 8-9, 11, 16-17, 19, and 26 as allegedly reciting non-elected species and holds the objection in abeyance until allowable subject matter is identified. Claim 9 has been canceled, rendering the objection moot with regard to this claim.

With regard to the remaining claims, as the objection is held in abeyance, Applicants submit that no amendment is necessary at this time.

III. Rejection under 35 U.S.C. §112, first paragraph

1. Enablement

All pending claims were rejected under 35 U.S.C. §112, first paragraph as not fully enabled by the specification. The Examiner alleged that the scope of the claims 1-4 were not commensurate with the disclosure of the specification. Applicants maintain that the specification adequately supports the complete scope of the claimed invention. However, without conceding the correctness of the Examiner's reasons for rejection, in the interest of advancing prosecution, Applicants canceled claims 3 and 4 and amended claims 1 and 2 to more clearly define what Applicants consider to be their invention. The amendment incorporates into these claims the limitations of claims 9, 10, and 24. Accordingly, claims 9, 10, and 24 were canceled. Other claims were amended to reflect this change. Assays and experiments to determine whether a substance is a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor were well established and known to one skilled in the art at the time of filing of the instant application.

The Examiner also alleges that the number of morphogens within the scope of the claims is large, and the combinations of target morphogens and molecules to be tested are numerous. Applicants submit that, while there are a number of morphogens, the known activities for these morphogens are similar enough that the assays described in the specification of the present invention are sufficient guidance to allow practice of the claimed invention. Applicants submit that the claims relate to potentiating morphogen activities, and do not necessitate one to determine which morphogen is being affected by the method. Please note that Applicants have amended claim 1 to recite "a morphogen activity." Therefore, one skilled in the art practicing the invention shall be focused on an activity known to be associated with a morphogen.

The Examiner states that Kim only shows that the effect of BMP-7 is enhanced, and not necessarily that this enhancement comes from overcoming inhibition of BMP-7 activities. Contrary to the Examiner's observation, the reference shows that activation of ERK2/MEK1 pathway by FGF inhibits BMP-7-induced dendritic growth (Figure 8). Therefore, inhibiting

ERK1/MEK1 will relieve the inhibition of effects of BMP-7. Nevertheless, Applicants have amended the claims to recite specific molecules, namely a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor. Therefore, the experimental results of Kim are no longer applicable to the claims of the present application.

The Examiner alleges that the specification's disclosure regarding dosage or administration route does not adequately support and enable the claims. Applicants respectfully traverse this ground of rejection. Such evaluation, in addition to the guidance given in the specification, is considered to be standard in art. See, for example, Benet, Øie, and Schwartz in Goodman and Gilman's The Pharmacological Basis of Therapeutics, 9th edition, 1996, p. 1707-1711. Thus, such decisions are made by the prescribing physicians routinely, and do not require undue experimentation.

The Examiner alleges that the in vitro/in vivo correlation that Applicants demonstrated in their January 22, 2004 response to the August 27, 2003 office action is not applicable to the present application because the cited references do not show administration of a molecule that overcomes morphogen inhibitor or a composition comprising such a molecule. Applicants submit that these references are directly relevant to the present application because the they demonstrate that the in vitro model systems used to quantitate growth of nerve cells, which are same or similar to the systems used in the specification of the present application, show good correlation with in vivo observation. The Examiner cites a review by Lo which makes a general statement regarding the correlation of in vitro and in vivo results to support her view that the state of the art was such that in vitro results did not translate directly into the clinic. Applicants maintain their previous interpretation of Lo, which is that Lo's discussion is primarily about the correlation of genetic markers and/or expression levels of proteins with a disease. Furthermore, Applicants have demonstrated that, regardless of the general assertion by Lo, in the particular experimental system that Applicants have used and described in the specification, there is a reasonable correlation between in vitro and in vivo results. Applicants do not assert that all in vitro results show reasonable correlations with in vivo results, just that the particular system described in the instant specification show a reasonable correlation with in vivo results, as demonstrated by the references previously cited by Applicants.

Applicants agree with the Examiner that Chung and Clari are about the correlation between the in vitro model and in vivo efficacy of treatment of heart failure. Applicants maintain that the correlation between an in vitro model and in vivo results for one type of tissue or one type of in vitro model is not a reflection of another type of tissue or another in vitro model. As explained above and in the previous response to an office action, Applicants demonstrated that the particular in vitro system described in the specification demonstrates a reasonable correlation with in vivo results. Should the Examiner maintain her rejection based on this ground, Applicants respectfully request that the Examiner show evidence contrary to the references that Applicants have brought to her attention.

The Examiner maintained her rejection based also on previously cited Halliday, Steece-Collier and Feigin, each of which Applicants have explained in the response to the previous office action why is inapposite as the bases for the Examiner's rejection. The Examiner states in this office action that these references were cited simply to indicate the state of the art at the time the application was filed, part of which was, as the Examiner states, that the neurodegenerative diseases are recalcitrant to treatment. Applicants respectfully submit that their invention addresses the problems faced by the state of the art at the time the application was filed, by teaching new methods and compositions for, among other things, treating neurodegenerative diseases. The references cited by the Examiner do not detract from the teachings of the present application. Halliday only discusses one approach to Alzheimer's disease, which is to consider the aspect of the disease related to plaque formation. It does not say other methods are ineffective. Steece-Collier indicate that counteracting neuronal degeneration would prevent manifestation of Parkinson's disease, which is in accord with the present invention. Feigin also shows that neuroprotective therapeutics are promising and effective when used to treat neurodegenerative diseases and the merits of treatments based on disease mechanisms. Therefore, Applicants maintain that these references do not support the Examiner's contention that the state of the art was so ill developed that the disclosure of the present specification do not enable the claims as proposed. However, in the interest of advancing the prosecution, without conceding the correctness of the Examiner's argument, Applicants canceled claims 3 and 4 without prejudice and amended claims previously dependent on these claims. Accordingly, rejections based on this ground is now moot.

2. Written description

All pending claims were also rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges that the examples of molecules that could overcome morphogen inhibition is not adequate written description of the entire genus of molecules.

Applicants maintain that the specification adequately supports the complete scope of the claimed invention. However, without conceding the correctness of the Examiner's reasons for rejection, in the interest of advancing prosecution, Applicants amended the claims to reflect specific molecules subject to this invention and the specific functions that it may have.

IV. Rejection under 35 U.S.C. §112, second paragraph

All pending claims were also rejected under 35 U.S.C. §112, second paragraph, as being indefinite and failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

Applicants amended the claims to more clearly describe what they consider to be the claimed invention. Claim 1 now recites "a morphogen activity." While a morphogen may possess many physiological activities, the known activities are well documented and defined. Claims 1 and 2 have been amended and no longer recites the phrase "morphogen inhibition." Each claim now recite "inhibition of the morphogen activity" and "inhibition of growth-promoting effects of endogenous morphogen," each of such activity is known in the art. Applicants submit the scope of the amended claims is therefore definite.

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Applicant believes no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P01-569 from which the undersigned is authorized to draw.

Dated: December 27, 2004

Respectfully submitted,

By_____

Erika Takeuchi
Registration No.: 55,661
ROPES & GRAY LLP
45 Rockefeller Plaza
New York, New York 10111-0087
(212) 497-3625
(212) 497-3650 (Fax)
Attorneys for Applicant